THE ACTIVE RESPONSE OF CAPILLARIES OF FROGS, TADPOLES, FISH, BATS AND MEN TO VARIOUS FORMS OF EXCITATION

A DISSERTATION

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BY

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I. EXCITATION BY ELECTRICITY

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The purpose of the experiments reported in this paper was to ascertain whether capillaries actively respond to localized stimulation, and it has been found that this is the case.

Using Lombard's method, one can see the capillaries of the human skin. Studies of the response of capillaries to excitation are no longer limited to animal tissues, nor will one be satisfied with the color reaction, as it is now possible to obtain a direct observation of the human capillary, and, under certain conditions, as Danzer and Hooker (12) found, even to see the movement of the blood corpuscles in the human body. Nevertheless, it is of value to study the behavior of the capillaries of animals for each tissue has its advantages and peculiarities. Although it has been suggested from time to time that capillaries may play an active part in propelling the blood, the generally accepted view has been that capillaries are entirely passive, and that the pressure and rate of flow of blood through them is controlled by the general arterial blood pressure, and the contraction and dilatation of the arterioles supplying the region. In recent years, however, evidence is accumulating which shows that capillaries can actively change their caliber, that they are controlled by nerves, and that they may play an important part, independently of arterial reactions, in the regulation of the distribution of the blood.

It is well known that there is an accelerated blood flow through an organ during its functional activity. Here what is important is the increased amount of blood passing through the capillaries, for in the capillaries takes place the exchange of gases, hormones, hormosomes and other materials needed for metabolism, and sometimes the distribu-

tion of substances, needed for preventive or curative purposes. For this reason, in a functioning organ, not only the size of individual capillaries, but also the number of capillaries through which the blood is flowing is increased to meet the need. Thus Krogh (1) has found that in resting muscles of frogs many capillaries are occluded, that as a result of activity the number of patent capillaries is enormously increased, and that in working muscles capillaries show a greater diameter. It is probably true of the human body that the nutrition of living cells depends largely on the efficiency of that part of the blood vessels with which the tissue function is most intimately concerned.

Not only does the condition of the capillaries of a tissue help to determine the blood supply to that part but the size of the capillaries has a marked influence on the general circulation. Examining the web of the frog, for example, the observer will note how great is the number of capillaries. He will also appreciate how large a proportion of the total blood can be contained in the capillary region of the vascular system, and how an increase in the diameter of the capillaries, if it occurs in a large part of the body, would absorb a large fraction of the total blood. The amount of the blood driven out by the heart in each beat, depends upon the amount entering its ventricles in diastole, so that if there is any accumulation in the periphery, the circulating blood is decreased and the blood pressure falls. This would be very significant if the enormous capacity of the capillaries were increased by some means, for instance, by toxic products from injured tissues, as mentioned by Bayliss (2), and Lee (3), and in the case of "histamine shock," by Dale and Laidlaw (4). Recently the direct observation of capillaries has stimulated a clinical interest in the condition of capillaries in many diseases. In the past three years many papers have appeared dealing with capillary pressure, and the circulation of blood in capillaries in diseased conditions, such as nephritis, arterio-sclerosis, shock and cardiac decompensation.

Any condition altering the nutrition of a tissue must have some vital relation to the capillaries and probably there are not only close interrelationships between capillary efficiency and certain diseases, but also between the latter and the active response of capillaries. It is hoped, therefore, that studying the active response of capillaries to excitation, may throw some light on the index of capillary efficiency, and consequently on the field of medicine.

Although the work of a number of observers has made it probable that the endothelial cells of the walls of the capillaries play an active

part in the regulation of the circulation, the view is not universally accepted. Very recently, for example, Friedlander and Lenhart (5) pointed out that "overwhelming proof has not yet been assembled in favor of the independent contractility of capillaries." There is no definite evidence that the capillaries of man are capable of actively changing their caliber. Any contribution giving evidence on this important question should be of value, and especially, because of its clinical significance, information is needed concerning the response of human capillaries to stimulations.

Structure of capillaries. Apparently some experimenters in this field have failed to make a sharp distinction between arterioles, capillaries and venules, and it is necessary that the writer should state at the outset his conception of the term capillary. Ranvier's view, that the capillary begins where the muscular coat of the artery ends and ends where the muscular coat of the vein begins, is probably correct, except that the venule should be considered to begin, as Hooker (38) points out, when the endothelial cells of the capillary begin to acquire a connective tissue sheath. Capillaries are therefore to be defined as tubes composed of bare endothelial cells, which are a continuation of lining cells of the arterioles and venules. The form of the endothelial cells varies according to the diameter of the capillary. Usually they are of irregular, oblong shape. The protoplasm of the endothelial cells is homogeneous, or presents some granulations in the neighborhood of a nucleus.

"The capillaries accommodate themselves to the shape of the elements of tissues or organs in which they are situated. In the muscle and nerves, they form a network with oblong meshes" (6). In the papillae of the human skin, capillaries are arranged in the shape of loops.

Schäfer (8) states that capillaries receive nerve fibers, which form a plexus of fibrils in close relation to the endothelial cells of which the walls of the vessels are composed, but contacts between the endothelial cells of blood capillaries and nerve-fiber endings have not been generally recognized, although there is physiological evidence that capillaries are controlled by nerves. Hooker saw contraction of capillaries of the ear of the cat on excitation of the cervical sympathetic nerve. Krogh (25) mentions that there are nerve endings in the capillary walls, and in a recent paper Krogh and others (39) state that capillaries and arteries in skin and muscle of the hind legs in frogs are innervated through sympathetic fibers, and through posterior root fibers.

The work of others. The review of the literature given by Hooker (30), (38), is so complete that only a summary of some of the evidence relating to the active response of capillaries to direct excitation is necessary.

Certain authors have accepted the idea that change in the size of capillaries is merely passive. For example, Natanson (9) concludes that capillaries cannot be filled except under the influence of arterial pressure. Without the latter, the capillaries collapse passively. Employing the method of von Kries (10) Natanson took for his criterion the complete blanching of the skin. The inadequacy of this method had been pointed out by Lombard (11), who found that the pallor of the skin is not necessarily associated with a cessation of flow of blood in the superficial capillaries. Danzer and Hooker (12) also failed to confirm his observation, and believed that the inadequacy of the criterion used by Natanson was sufficient to explain his results.

On the other hand, there is considerable evidence which goes to show that capillaries actively respond to stimulation. In 1865 Stricker (13) observed capillaries in the nictitating membrane of the frog to dilate and to constrict. In the following year, Stricker (14) modified his technique by examining the isolated nictitating membrane in aqueous humor. When the membrane was exposed to ammonia vapor for three or four seconds, and then examined under the microscope, he saw the capillary lumen almost disappear and then enlarge. He also obtained positive results by electrical stimulation. When the capillaries contracted they became invisible.

Golubew (15) confirmed the observation that capillaries change their size under various conditions, and regarded these changes as due to certain spindle elements. Rouget (16) described perivascular cells which he regarded as the agents causing the alteration of the size of the capillary. Severini (17) claimed that the application of CO_2 caused capillaries to dilate, while oxygen made them contract. But Severini's experiment was not confirmed by Tarchanof (18) nor by Roy and Mehring (19).

Golubew's view was adopted by Tarchanof who employed alcohol, ether, ammonia, ferric chloride, acetic acid, and heat to stimulate capillaries. These procedures, according to him, aroused the so-called spindle elements to swell, thus occluding the lumen.

Roy and Brown (20) attempted to measure the blood pressure in capillaries. They were convinced by their observations that capillaries possessed active contractility. They saw that local anemia, produced

by compression of an area, was followed by hyperemia, accompanied by a dilatation of arterioles, venules and capillaries. Dilatation of capillaries was also seen on the application of chloroform. They concluded that it was not the spindle elements of Golubew, but "it is by the contractility of the capillary wall as a whole, that the diameter of the vessel is changed." They also mentioned that the congestion which followed the compression of a portion of the web was an active change, because the dilatation of the capillaries was greater than could be explained by the increase of their internal pressure.

Roy and Brown gave further evidence that the contraction and dilatation of capillaries were not merely caused by changes in pressure. They found that there was little difference in the size of the capillaries before and after the frog's leg was amputated. By the application of chloroform and tapping the abdomen, the capillaries remained dilated with a low intracapillary pressure. Again, the effect on the caliber of the capillaries, of raising the extra-capillary pressure was usually very slight.

Krogh (1) has pointed out that the pressure necessary to force muscle capillaries to open, when they are actively contracted, is very much higher than the normal arterial pressure, and that capillaries do not contract measurably by elasticity when the pressure is reduced by closing or cutting the arteries. This is better understood if one recalls that though large thin walled rubber tubes collapse when internal pressure is withdrawn, this is not true of smaller tubes, and tubes as small as capillaries in spite of the delicacy of the walls, might keep open even with no internal pressure.

A paper by Steinach and Kahn (21), though largely concerned with repetition of earlier work, is interesting. They employed the cut nictitating membrane of the frog. Steinach and Kahn saw the perivascular cells described by Rouget (16), and adopted the view that the perivascular elements were responsible for capillary constriction.

If a blunt pointed instrument is drawn across the skin, a white line is left, which turns to red in a few seconds. Marey explained it as due to a localized contraction and dilatation of capillaries. But Bloch (23) thought there was only evidence of capillary constriction. Slade, Cotton and Lewis (24) saw the reaction well developed in cases of "irritable heart" and adopted the view that it was a capillary phenomenon.

Krogh (25) reported that scratching an area on the frog's tongue causes dilatation of capillaries and arterioles, usually over an area greater

than that which had been stimulated. He concluded that the reactions of capillaries could be independent of arterial pressure. The effect of electrical stimulation on arterioles was inconstant, and the effect of an electrical current on capillaries was very doubtful. He found that pure CO_2 caused dilatation of both arteries and capillaries. In general, all the substances tested by him gave the same effect on the capillary wall; relaxation of its powerful tone, which it acquired again after a period of several minutes. He was convinced that the spreading of the effects of stimuli was an axone reflex. He also found (26) that the skin capillaries of the frog react to mechanical and chemical stimuli independently of arteries, but to a less degree than those of the tongue, and that single capillaries undergo spontaneous changes in diameter.

Another proof of the independent contractility and dilatation of capillaries was also given by Dale and Laidlaw (27) and Dale and Richards (28). They pointed out that histamine when injected into the circulation of cats, caused dilatation of capillaries, together with constriction of aterioles. This was confirmed by Rich (29), Doi (37) and Hooker (30). Hooker also found that the injection of histamine destroyed the response of capillaries to electrical stimulation of the sympathetic nerve. Hooker described the post-mortem changes of capillaries of the cat's ear, showing the independent action of the capillaries. Such post-mortem changes of capillaries were also abolished by the injection of histamine (30).

Methods. In one series of the writer's experiments, the capillaries were excited by elcctricity. The same induction apparatus was employed in the experiments on frogs, bats and men. It consisted of a primary coil of 680 windings, and a secondary coil of 5000 windings. One, or in some cases, two dry cells were connected in the primary circuit. A different coil was used in the experiments on tadpoles and fish.

When the direct current was used it was obtained from one or two dry cells, or from a generator giving 60 volts. When the latter was used, the strength of the current was modified by shunting a part of it through a rheostat. A milameter in the circuit measured the strength of the current, and a commutator permitted the direction to be changed.

In order to localize the stimulations, unipolar methods were employed. When the induction current was used, the indifferent electrodes was connected to one pole of the induction apparatus, the other pole being left free, as a rule. The active pole was in many of the experiments a fine platinum wire, soldered to one end of a brass wire, the other end of which was either left free, or in case a stronger current was needed, con-

nected to an insulated sheet of metal, or to the observer's body, to enlarge the surface to be charged.

When the direct current was employed, some of the experiments were made with polarizable, and some with non-polarizable electrodes. When the non-polarizable electrodes were employed, the indifferent pole was a Harvard boot electrode resting on moist gauze connected with the body of the animal, and the exciting pole was a fine pointed camel's hair brush, which was fastened into one end of a glass tube by a plug of kaolin, moistened with physiological salt solution. The tube contained a solution of zinc sulphate, and an amalgamated zinc rod, which was connected by a wire with the battery. In some cases the camel's hair brush was tied to the tip of a Harvard boot electrode.

In order that the exciting electrode might be adjusted accurately, and so as to exert the least possible pressure on the capillary to be excited, it was supported by a binding post, which was clamped at the extremity of a straight rod, which was fastened to the vertical arm of an L rod, which was fastened by a clamp to a short rod projecting downward from a plate screwed to a microscope, in the ordinary position of an objective. By sliding the microscope on the table, by lateral movements of the horizontal rod, and by use of the adjustment screws of the microscope, the active pole could be brought in contact with the skin over the desired capillary, without exerting undue pressure.

Experiments on the web of frogs. The frog was pithed and the skull cavity plugged with a match to prevent loss of blood. The animal rested on a frog board. One web was spread out and fastened with threads tied to the tips of two toes. Beneath the web there was a hole in the board to let the light come through. The web was below the heart level. The spinal reflex effects which might result from excitation, on the vessels in general, as well as on the vessels of the part studied, can be avoided by the section of the sciatic nerve. This was done in many of the experiments. It had the advantage of also preventing reflex movements of the limb when the excitation was given. It was recognized, of course, that it would cause vasodilatation and subject the capillaries to an unusually high blood pressure. This was, however, regarded as an advantage. If in spite of the high blood pressure, a capillary could contract when excited, the result would be more striking.

In addition to the effect of cutting the nerve, the condition of the web, too dry or too wet, the spreading of the current, the mechanical influence of the exciting pole, pressure upon the leg, stretching of the web and other influence might become sources of error. When the active pole is

fine enough and is adjusted so as to barely touch the skin over a single capillary, when the current is very weak, and the web just a little moist, and when other conditions are suitable, the sources of error appear to be under control.

Effect of a tetanizing induced current. One pole of the secondary coil of the induction apparatus was connected to a copper plate, the indifferent electrode, and the other pole was left free. The frog rested on a pad of wet gauze which was on the copper plate.

An eyepiece micrometer was employed, not only for measurement, but also for locating the stimulated point of one capillary easily and definitely. The active pole, the fine platinum wire was screwed down slowly until it just touched the skin exactly over a single capillary. In order to be sure that the result was not caused by a mechanical effect, the writer waited ten minutes before applying the current. Then the key was closed for about half a second. When the unipolar current was weak, there was no visible effect. If the current was strengthened, by enlarging the surface to be charged, the circulation of the stimulated capillary was seen to slow. A still stronger current was obtained by connecting the other pole of the secondary coil to the ground, and this strong excitation stopped the blood flow in the stimulated capillary. At that time the circulation in other vessels in the field was normal. Finally, the blood flow in the excited capillary recovered. Many experinents were made, and others were called in to verify the observations. Some of the results may be illustrated in fig. 1.

Capillary *A* was stimulated at the point *a*; the automatic interrupter was started by closing the key for half a second. The local flow of the capillary *A* gradually slowed, then ceased, while the blood flow in *B* and other capillaries continued as usual. Eight minutes later the circulation in *A* returned.

In a similar way capillary *B* was excited. *B* was stimulated with the same strength of current but for a longer time.

After 3 seconds the circulation in *B* began to slow.

After 18 seconds the circulation in *B* stopped.

After 9 minutes the circulation in *B* recovered.

As has been said, that effect was strictly localized. For instance, when the circulation in the upper part of *B* was stopped there were still corpuscles coming from the capillary *F* and flowing toward *G*, while above the stimulated point *b*, which was contracted and so blocked without the blood being coagulated, a few corpuscles oscillated between *h* and *b* and went back and away through *A*.

Effect of infrequent induction shocks. The arrangement of the apparatus, and the method of excitation, were the same as before, except that the battery and key were connected with different posts of the primary coil so that separate induction shocks could be given.

The results of the tests illustrated in figure 2 were as follows:

Capillary A was stimulated at the point a. Tapping the key three times during 5 seconds did not cause a visible effect.

Capillary A was excited at a by twelve makes and breaks during ten seconds.

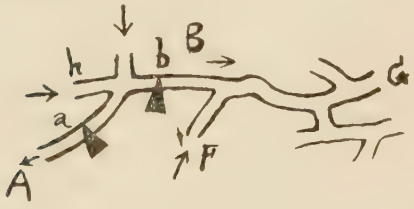

Fig. 1

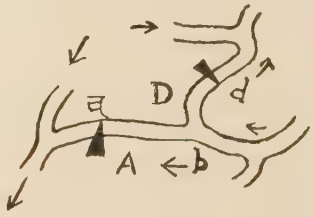

Fig. 2

Fig. 1. Capillaries A, B, were stimulated one after another. Arrows show the direction of the circulation. Triangles show the points where the active pole touched the skin over the capillary.

Fig. 2. Capillaries A and D were stimulated one after the other with infrequent induction shocks. Triangles show the points where the excitations were applied to the skin over this capillary.

After 5 seconds flow in A was slowed, but was normal in D.

After 12 seconds flow in A stopped.

After 16 seconds flow in A recovered.

After 2 minutes flow in A ceased again, but was normal in D.

After 3 minutes flow in A recovered again.

After 5 minutes flow in A stopped again.

After 10 minutes flow in A recovered again.

Capillary D was stimulated at d. Single make and break did not produce effect. Fifteen makes and breaks during 5 seconds gave the following:

After 4 seconds the flow slowed.

After 10 seconds the flow stopped, but was normal in A.

After 20 seconds the flow in D recovered.

After 1 minute the flow in D ceased again.

After $2\frac{1}{2}$ minutes the flow in D recovered again.

The repeated cessation and recovery of the local circulation suggested a rhythmical response of the stimulated capillary. When *A* was excited, one or two corpuscles passed the point *b* several times, but could not get through *a*. They showed to-and-fro movements between *a* and *b*, then went back through *D*. Apparently in such a case the constriction was localized at the middle of the excited capillary, at the point *a*, and the stopping of the flow could not be due to a constriction of the arteriole, because there was still movement of corpuscles between *a* and *b*, as well as through *D*, which was supplied from the same arteriole.

Repeated responses of capillaries have been described by others. In this case the nerve had been cut, so this must be regarded as a peripheral phenomenon. Looking at an unstimulated area, sometimes one could see the cessation of blood flow in one then in other capillaries. In this particular case, however, the repeated cessation and recovery were seen in the stimulated capillary, but not even in the neighboring ones supplied from the same arteriole.

Excitation by galvanic current. Two dry cells were used. The indifferent electrode was connected with the anode, the stimulating electrode with the cathode. When several excitations were given, the key was closed for a short time, opened and immediately closed again for a second period, and so on. The following effects were noted, the time of appearance of effects being estimated from the last closure of the key:

Capillary *A*. One excitation given during 1 second:

No effect.

Capillary *B*. Eight excitations given during 5 seconds:

Flow slowed after 7 seconds.

Flow stopped after 22 seconds.

Flow recovered after 24 seconds.

Capillary *C*. Ten excitations during 4 seconds:

Flow slowed after 8 seconds.

Flow stopped after 20 seconds.

Flow recovered after 3 minutes.

The current was reversed, so that the active pole became the anode, and another series of experiments was made. A part of the series may be tabulated as follows:

Capillary *A*. Eight excitations during 4 seconds:

Flow was slowed after 7 seconds.

Flow stopped after 15 seconds.

Flow began again after 2 minutes.

Flow normal after 3 minutes.

Capillary *B*. Twelve excitations during 5 seconds:
Flow was slowed after 10 seconds.
Flow stopped after 15 seconds.
Capillary *C*. Fourteen excitations during 7 seconds:
Flow was slowed after 10 seconds.
Flow stopped after 30 seconds.
Flow began again after 32 seconds.
Flow was normal after 39 seconds.
Capillary *D*. Twenty excitations during 8 seconds:
Flow was slowed after 15 seconds.
Flow stopped after 3 minutes.
Flow began again after 5 minutes, 25 seconds.
Flow stopped again after 6 minutes.
Flow started again after 6 minutes, 30 seconds.

In the case of *A* and *B*, the stimulated capillary was packed with stagnated corpuscles. In the case of *D*, a comparatively frequent excitation aroused repeated response.

In the following experiments non-polarizable electrodes were used. The active pole was the cathode. The results of a part of the tests were as follows:

Capillary *N*. With one cell, ten excitations in 1 minute:
No effect.
Capillary *O*. With two cells, four excitations in 1 minute:
Flow slowed after 1 second.
Flow became normal after 23 seconds.
Capillary *P*. With two cells, four excitations during 1 minute, 30 seconds:
Flow stopped immediately.
Flow started after 86 seconds.
Flow normal after 4 minutes.
Capillary *R*. With two cells, four excitations during 80 seconds:
Flow stopped immediately.
Flow started after 162 seconds.
Flow normal after 4 minutes, 30 seconds.
Capillary *S*. With two cells, four excitations during 80 seconds:
Flow stopped immediately.
Flow started after 162 seconds.
Flow normal after 4 minutes, 30 seconds.

In the case of *P*, a very localized constriction was observed. With non-polarizable electrodes at least two dry cells were needed. Experi-

ments seemed to show that a longer duration of excitation tended to prolong the cessation of corpuscular flow in stimulated capillary.

Experiments on the fin expansion of tadpoles. These, with the experiments on fish were made at the Marine Biological Laboratory in Woods Hole.

Method. A somewhat different method was employed from that which was used in the experiments on frogs. An upright chamber was made, such as Professor E. R. Clark (27) found useful in studying lymphatics. The back of the chamber consisted of a glass slide, 39 × 75 mm; the front, of cover glass; the sides and bottom, of three narrow strips composed of two thicknesses of window glass; and all of these were cemented in place with canada balsam, the top being left open. The floor of the chamber was coated with a film of paraffin.

In experiments the slide was clamped to the stage of a microscope, which was arranged with the tube horizontal. The tadpole, to be examined, was anesthetized in a dish of chloretone solution, of a strength of 1:3000, or 1:6000, and then transferred carefully from the dish to the cell by means of a medicine dropper.

The tadpole was brought carefully to the side of the chamber next to the cover glass by means of a blunt needle. A narrow piece of cover glass was set on the floor of the chamber, leaning against the cover glass which formed the front wall, and was brought against the tail of the tadpole by pressing gently with the blunt needle. Since the narrow piece of cover glass came in contact with the thick, central, muscular portion of the tail, pressure on the fin expansion of the tail was avoided.

By using the upright chamber, the tadpole could remain in its normal position, so experiments of long duration were possible, without the complications which might result from an abnormal position. The apparatus for adjusting the active electrode was the same as described already, except that it was arranged with the tube of the supporting microscope in the horizontal position. In this way the stimulating electrode could be moved backwards and forwards.

The indifferent electrode was brought in contact with the fluid near the body of the tadpole, the fluid itself really becoming the indifferent pole. The stimulating electrode reached the fin expansion of the tail from the right corner of the chamber. A tetanizing current was employed.

In a number of cases, the blood stream in the stimulated capillary became slow, but did not stop. In a few cases, however, the circulation stopped at the place where the capillary was excited. In four cases,

changes of shape of corpuslces passing the stimulated part of the capillary were clearly observed. It was possible with an upright chamber so constructed, to make experiments with the highest powers of the microscope, even with the oil immersion. The endothelial cells of the capillary wall could be well observed. Sometimes after the application of the stimuli, the stimulated capillary disappeared from view under the low power, but was still to be seen with the highest power and looked narrowed.

Experiments on the caudal fin of fish. When the writer was working at the Marine Biological Laboratory in Wood's Hole, he found that some of the fish could be used to advantage for studying the response of capillaries to excitation.

The technique used was very simple. The unipolar method of excitation was employed. The fish was placed on a glass plate. A mass of moistened filter paper acted as the indifferent electrode. The active pole, the holding and adjusting apparatus were the same as described already. The fish was usually anesthetized with chloretone. Unanesthetized fish were also used in a few experiments of short durations. The fish were kept moistened.

Experiments were made on the caudal fin of Fundulus heteroclitus and Cyprinodon variegatus, and also on the skin capillaries of the abdomen of the small toad fish. The capillaries actively responded to the tetanizing current and to a series of separate induction shocks, or to excitations with the direct current.

The corpuscular flow in the stimulated capillary became slow and then stopped. The relation between the duration of the excitation, and that of cessation of circulation in the stimulated capillary was irregular. With the same duration of excitation, the results were not exactly the same. The response of the excited capillary, however, was always strictly localized.

Experiments on the wing of bat. Among warm-blooded animals, bats possess the advantage for our purpose of having transparent wings and of belonging to the mammals. The bats were hibernating, and were kept in a cold room. When used they were aroused from their sleep by the handling. They were etherized, and the wing to be examined was placed so that it was below the heart level.

The bat was placed on his back, on a suitable holding board. The left wing, which was to be studied, being stretched across a hole in the board. The stimulating electrode was brought to touch the wing either from above or below. The unipolar method, as described for frogs, was used.

Influences affecting the resistance to the flow, and spreading of the current had to be considered. It was found that the bat's wing which is coated with keratin substance has greater resistance than the frog's web. A strength of current that would alter the flow of the blood through the frog's web failed to be effective in the case of the bat's wing. When the current was strong, there was an effect, but there might be a tendency to injure the tissue, and so too strong currents had to be avoided. When the bat's wing was moistened with water, it appeared to gather together in fine droplets, which, if sufficiently numerous, formed a sheet of water. If the active pole touched a layer of water, the current spread, and was not so effective as when the current was condensed at a very fine point.

In as much as disappearance of blood from a capillary was assumed to be evidence that it was contracting, the level of the capillaries with respect to the heart was important. When the vessels are above the heart level, constriction of the arteriole may empty them. Hooker (30) made the following experiment: A cat was placed on an animal holder; the capillaries of the ear were about 3 cm. below the heart level. The arterial supply to the area under observation was mechanically shut off, so that there was no movement of red cells in the capillaries, but the latter vessels did not empty. As the part to be stimulated in my experiments was always below the heart level, constriction of the arteriole alone could not empty the capillary, and this error of experimental procedure was certainly avoided.

At first the picture was not so clear as in the frog's web, but with practice one could overcome the early observational difficulties. Instead of giving a net-like appearance, as in the case of a frog's web, the capillaries of the bat's wing are longer, and look like the small branches of a tree. In some cases the presence of capillaries was indicated only by a stream of corpuscles; while in other cases a faint line representing the capillary was seen though there were no corpuscles then present. To be sure that the vessels to be excited were not arterioles or venules, the smallest capillaries were chosen for excitation.

The tetanizing current did not cause any visible contraction of the bat's capillary, when the strength was enough to excite the capillary of the frog's web. Even when one pole of the secondary coil was connected with the active electrode there appeared, except in one case, no change in the microscopic field.

Excitations with infrequent induction shocks. When one pole of the secondary coil was connected to the indifferent pole, while the other

pole was left free, and the brass wire to which the stimulating electrode was soldered was also free, no result was obtained. Even when the active pole was connected to the operator's body, closing and opening the key once did not arouse the contraction of the bat's capillary. When, however, the key was opened and closed twice at 3-second intervals, a distinct slowing of the circulation was observed. The following is a typical experiment (fig. 3):

Capillary *A*. Stimulated at point *a* by closing and opening the key three times at intervals of 3 seconds.

After 1 second flow in *A* slowed.

After 145 seconds the corpuscles came through in single file slowly, but continuously.

After 180 seconds corpuscles came through at intervals.

After 223 seconds the blood flow in capillary *A* stopped but was visible in neighboring capillaries.

Fig. 3

Fig. 4

Fig. 3. Capillaries *A* and *B* were stimulated one after another, at points *a* and *b*.

Fig. 4. Showing alteration in form of corpuscles when passing the excited region, about the middle of capillary *P*.

After 264 seconds the flow was restored, corpuscles coming one by one or in small groups.

Capillary *B*. This was stimulated at the point *b* by closing and opening the key three times at 3-second intervals.

After 134 seconds corpuscles came through at intervals.

After 185 seconds, blood flow in *B* reversed.

After 203 seconds, flow in *B* stopped, but was visible in neighboring capillaries.

After 275 seconds, one corpuscle moved to and fro between *b* and *c*, and then forced its way through the stimulated point *b*; then four or five corpuscles followed, one by one; then the circulation stopped again; then four or five corpuscles forced their way through *b*.

The most constricted part probably was the point *b*, where the current was condensed. This was shown by the to and fro movement of the corpuscles between *b* and *c*, and by the fact that the corpuscles could pass the point *b* only with difficulty. As soon as they passed *b* they

went through freely. This observation also showed that the most apparent response was limited to the part stimulated, about the middle of the capillary *B*.

Excitation by the direct current. The electric current was supplied from a dynamo giving sixty volts. A mercury key permitted the current to be sent through a rheostat, where it was shunted, so that any desired amount could go through a milameter, and then by way of a commutator, which allowed the direction of the current to be changed, to the indifferent pole, which was the cathode, or in case the current was reversed, the anode. The current was closed for a brief time, then opened and closed for a brief interval again, so that a series of excitations was given.

In the following tests the active pole was the cathode. A few of the tests are recorded below.

Capillary *L*. Two closures of the key during 10 seconds.

No effect.

Capillary *M*. Four closures in 1 minute.

After 10 seconds, flow was slowed.

After 20 seconds, flow was normal again.

Capillary *N*. Four closures in 3 minutes.

After 2 seconds, flow stowed.

After 5 seconds, flow stopped.

After 69 seconds, corpuscles oscillated.

After 135 seconds, flow normal.

Capillary *P*. Four closures in 3 minutes.

After 11 seconds, flow slowed. Corpuscles changed their shape when passing through the middle of the capillary.

After 16 seconds, flow stopped.

After 82 seconds, corpuscles oscillated.

After 130 seconds, flow normal.

Capillary *R*. Four closures in 3 minutes.

After 4 seconds, flow stopped.

After 80 seconds, corpuscles oscillated.

After 310 seconds, flow normal.

In this experiment too, the corpuscles were seen to alter their form in passing through the constricted area.

In the case of *L*, in which the current was closed and opened twice during 10 seconds, no effect was seen. In the case of *M*, in which the current was made and broken four times during the course of one minute, the flow was slowed. In the case of *N* in which four closures were made

during 3 minutes, the circulation in the stimulated capillary was slowed and stopped. According to the general law of polar excitation of nerve and muscle, as recognized by Pflüger (7) and Von Bezold (34), the effect of stimulation appears at the cathode upon making, and at the anode upon breaking the current. The present experiments tend to show that the duration is important. This is, however, not striking if one considers the cases given by Kühne (35), and Verworn (36) for they show that the constant current stimulates throughout the duration. The experiments on *N*, *P* and *R*, when the current was given in the same manner, showed different effects.

The experiments on *P* and *R*, were observed under high magnification, and the shape of the corpuscles were seen to be changed as they passed through the stimulated part of the capillary. Corpuscles, when they were passing the excited region, about the middle of capillary *P*, for example, one by one altered their form, and acquired a comma shape (see fig. 4). This suggested that the capillary was partially blocked by a very localized narrowing of the lumen, as if there was a protoplasmic protrusion of the endothelial cell. The protrusion, although it was not seen as such, forced the corpuscle to show a dent, which moved from one end of the corpuscle toward the other end, as the cell was passing the part.

In the case of *R* the corpuscle showed various changes when going through the affected part of a single capillary. It began to penetrate the partially blocked region with a narrowed end. When it had passed half way through the constricted area, the portion that had passed resumed its original shape, so that the corpuscle had a dumb-bell form. Then as the corpuscle continued to pass through, the hind end became narrowed. After the whole cell had passed the protoplasmic protuberance of the capillary wall, the corpuscle resumed its ordinary form.

In the case of *P* and of *R*, a localized contraction was observed.

Stimulation with non-polarizable electrodes. In this experiment the indifferent pole was a boot-electrode which rested on the moist cloth on which the bat lay. The active pole was a sharp brush, fastened to the end of a piece of glass tubing by a plug of kaolin. It is unnecessary to relate the results in detail; they were similar in character to those obtained when a polarizable electrode was used as the active pole.

Experiments on human capillaries. Method. The capillary loops of the human skin may be directly observed by following Lombard's method. This method consists of moistening the skin with a drop of glycerine or transparent oil, and observing by a strong light with a

microscope. A Zeiss binocular microscope has the advantage of taking any desired position, and affording a large working distance. The ordinary microscope is also of great service. The latter in practice was found more convenient for the localization of a particular capillary. When capillaries of the thumb are to be examined, one may turn the front edge of the stage of the microscope toward the finger. Too high powers have the disadvantage of losing definition and depth of focus. An artificial illumination is better than the day light, because the former can be more readily adjusted.

The writer stimulated and observed capillaries of his own finger, or of the back of his hand, either radial or ulnar side, or the skin of the fore arm. The fore arm rested on a wooden support, at one end of which there was a piece of wood which could be moved up and down to fit the palm. When the finger was examined, the arm support was used and the finger rested on the microscope stage. There should be no movement or tremor of the part to be examined, and no pressure should be brought on the blood vessels or nerves of the arm. As Danzer and Hooker (12) have pointed out, the part to be studied should be clean and free from moisture. The skin should be scrubbed with soap and water, then thoroughly dried. If there is moisture between the skin and oil, the field is less clear.

In case electrical stimulation was to be employed, a drop of glycerine instead of oil should be used. Some control experiments were made to test the conductivity of glycerine and oils. In the case of oil, the galvanometer oscillated but little, unless the electrode pressed heavily on the skin. As soon as the electrode touched a drop of glycerine the conductivity as indicated by the galvanometer was apparent.

The appearance of the superficial capillaries of the human skin. If Lombard's method be followed the epithelium is not seen, but the underlying corium with its papillae is observed. As the strong light penetrates a short distance into the corium itself, its connective tissue is sufficiently transparent to show the capillaries of the papillae. The condition of the skin determines the picture observed. Sometimes one sees only a few, and at other times many capillary loops against a pale yellow background. Sometimes the background has a rose tint, the red being unevenly distributed. Some of the loops are twisted on themselves, some capillaries look like simple arcs. While the loops of the ulnar side of the back of the hand are short, long loops are seen on the radial side.

Lombard observed a capillary loop communicating wtih a superficial veinlet, and that when pressure was brought to bear on the skin over the capillary loop, the side toward the vein emptied before the other side of the loop, which was undoubtedly in communication with an arteriole which was deeper down and not visible. The veins were more superficial, and the arterioles lay deeper down in the corium and could not be seen. The writer failed to see such venules in his skin, and the flow of the blood was too rapid to permit the direction to be observed, unless it was slowed by pressure, or by the constriction of the capillary caused by stimulation.

Sources of error in studying human capillaries. The movement and tremor of the field under observation might give a wrong impression. Care must be taken to distinguish the disappearance of a capillary caused by the stimulation, from that produced by loss of focus caused by movement of the part. After working several days continuously, one could locate and recognize a definite capillary more easily, and could tell the difference according to the following method. The capillary to be stimulated was in the same plane with at least some of the other loops. Before stimulation, control experiments should be made. Loops in the same plane would disappear, and reappear at the same time by changing the focus. If the disappearance is limited to one particular capillary while neighboring loops of the same plane are still visible, then it must result from stimulation.

The phenomenon of diasppearance was not the only kind of response caused by stimulation. Sometimes after stimulation the loop was still visible, but slow circulation resulted. Ordinary capillaries looked like continuous red threads, arcs, or loops, and no indication of corpuscular flow was observed, as the circulation was too quick to show individual corpuscles. After the application of stimulation, the red cells were seen streaming slowly through the capillary, and the flow of corpuscles was evident. Danzer and Hooker (12) have shown that the corpuscular flow was seen under pressure of 18 to 27 mm. Hg. In this connection care must be taken to avoid any pressure. It was not impossible to avoid pressure as the active pole was either a very slender wire or a delicate camel's hair brush and fine adjustments were provided. In as much as Lombard described a case of vasodilatation caused by pressure on a nerve, care had to be taken that this did not occur.

Danzer and Hooker found that it frequently happened that when one obtained a focus of the capillary field, one or more of the capillaries stood out conspicuously large. They stated that such capillaries

represented vessels in which the corpuscular flow had stagnated, and corpuscles were thickly packed together. Even a high extra-capillary pressure did not change the appearance of such vessels. Bearing this in mind, one would assume that the lack of visible change after stimulation in some cases might be due to the condition of the capillary.

The secretion of the skin might cause trouble. Clean and dry skin was required for obtaining a clear picture. When sweat intervened at the coil-skin boundary, the intimate penetration of the oil was interfered with, and the clarity of the field was lost. Indeed, sometimes, during the long experiments, the field became less clear, and one might mistake that the capillary under observation disappeared. This is, however, easy to differentiate. If it is due to the secretion of the skin, the picture will not become clear again unless the skin is cleaned once more. If it is a real disappearance, the capillary will reappear.

Excitations with a tetanizing current. The induction apparatus, dry cell, the electrodes and the key were the same as those employed in studying the bat's capillaries. The copper plate, which acted as the indifferent pole, was placed on a wet pad on the arm. As the writer worked on his own capillaries it was found to be more convenient to make the observations on the left hand. Capillaries stimulated with the tetanizing current did not show visible change.

Excitations with infrequent induction shocks. The part to be examined was about 12 cm. below the second intercostal space. The capillaries in the skin at the base of the nail of the ring finger, at the ulnar side, and at the radial side of the back of the hand, and in the skin at the lower part of the fore arm, were studied. The skin of the fore arm looked softer than that of the back of the hand, but the tremor caused by the pulse was greater.

A capillary on the back of the hand was chosen and watched for a while, and the condition of this capillary, and of the neighboring ones was noted. The active pole, the platinum wire, was adjusted to gently touch a point of the skin just over the capillary to be stimulated. Enough time was allowed to let the mechanical influence pass off, if there was any.

Single making and breaking shocks did not bring any visible response. The same capillary which did not respond to single shocks, was affected by a summating series. Before excitation, capillaries appeared as pink threads, no individual corpuscles being seen. The key was then closed and opened four times at an interval of two seconds each. The following was noted:

After 3 seconds, minute bodies, the red corpuscles, were seen moving along the stimulated loop, but no change in neighboring capillaries.

After 10 seconds, the minute bodies passed one or two at a time.

After 15 seconds, movements of bright minute bodies were followed by groups of corpuscles, the observations of the latter being facilitated by the former.

After 30 seconds, normal again.

In certain cases when the flow of the corpuscles was not seen, the part of a capillary stimulated merely appeared less distinct. For example, the writer in some cases saw at one point of the stimulated capillary a constriction, which broke the continuous appearance of the red loop.

In other cases, the constriction did not break the continuous outline, but before the application of the stimulation, the red color of the whole loop looked almost even, after the excitation, the color became uneven.

Evidently some change took place at the stimulated part of the capillary. The slowing of circulation might have been due to a localized constriction. Concerning the localized change of appearance of the red loop, one might think that the number of red cells passing the stimulated part might have been decreased as a result of increased friction.

The following experiments were made on the skin at the base of the nail of the ring finger of the left hand, the finger being 13 cm. below the second intercostal space. Groups of make and break induction shocks were used. The effects were confined to the capillaries which were excited.

Capillary *a* was excited eight times in 15 seconds. Circulation of capillary was slowed.

Capillary *b* was excited fourteen times in 13 seconds. Red color of the loop became uneven.

Capillary *c* was excited ten times in 18 seconds. Circulation of the capillary was slowed after 3 seconds.

Capillary *d* was excited ten times in 18 seconds. Blood flow of the capillary *d* was slowed after 10 seconds.

Capillary *d* was excited ten times in 15 seconds. The continuous appearance of the red loop was broken near the arc part.

Capillary *f* was excited twelve times in 15 seconds. No visible response.

Capillary *g* was excited twelve times in 15 seconds. Blood flow of the loop was slowed.

Effects of direct current. The electric current was supplied by a dynamo generating six volts. The stimulating pole was the cathode. As the active pole was polarizable the passage of the current caused the liberation of hydrogen gas, at this pole, often as fine bubbles which tended to obscure the field. The gas bubbles did not last very long, and experience made the field appear clearer. Nevertheless the latent period could not be accurately estimated.

After the application of a series of excitations, in some cases, the circulation of the stimulated capillary was slowed; in other cases, the capillary became less red at the arc of the loop. In still other cases, the stimulated capillary disappeared and reappeared.

Sometimes an appropriate stimulation caused a single capillary or a part of the capillary to disappear and reappear again and again. The duration was irregular, generally that of the disappearance was shorter. The disappearance was not due to constriction in the arterioles, which might have prevented the blood from reaching the vessels distal to the constriction, for the part under direct observation was below the heart level and the phenomenon was localized to the capillary that was excited, neighboring capillaries remaining unchanged. This would be impossible if the response was not given by the capillary itself.

In the following experiments non-polarizable electrodes were used. The stimulating electrode was the cathode. Instead of glycerine, a drop of 0.1 per cent or 0.2 per cent salt solution was put on the part to be examined as the latter conducted the current better. The brush was washed and moistened with the same solution. When one is accustomed to seeing the capillaries, they can be observed if the skin has softened by glycerine and oil for several days, even when a drop of water or very dilute salt solution is placed on the skin after oil has been thoroughly removed from the surface.

Sources of error. Under a drop of the dilute salt solution capillaries looked smaller and less distinct than when glycerine was employed. The skin became dry easily, and even before this, a concentration of salt solution may interfere with the picture. Sometimes the clarity of the field was lost entirely or partially. A partial loss of clarity might shade the capillary under observation. This must not be mistaken for the disappearance of the vessel. On the other hand a positive reaction might be mistaken to be negative when the phenomenon could not be clearly observed. In spite of the difficulties, the use of non-polarizable electrodes, because eliminating the gas bubbles, was advantageous. The difficulties were overcome by cleaning the field diligently, by renewing the drop of salt solution, and by untiring work.

In a number of experiments individual capillaries were stimulated with the same length of period but various numbers of excitations and the observed reactions were irregular.

The following experiments were made on the skin at the base of the nail of the ring finger of the left hand, the finger being 130 mm. below the second intercostal space. Non-polarizable electrodes were used.

The above experiments were made with the same length of period and the same number of excitations. The results, however, were different in various cases. One would think that conditions of various capillaries, or of one capillary at different moments, were not the same, which might determine the reaction observed. (Table 1.)

Discussion. *Is the absence of muscular coats unfavorable to the view that the blood capillaries have the power of active response to stimuli?* As the blood capillaries consist of endothelial cells, which are not as highly differentiated as muscular tissue, the old view assumes that

TABLE 1

CAPILLARY	NUMBER OF CLOSURES	PERIOD OF EXCITATION	OBSERVATIONS
		minutes	
R	8	3	Flow in capillary *R* slowed
R	8	3	No visible reaction
R	8	3	*R* disappeared and reappeared
R	8	3	Blood flow in the single capillary slowed
Z	8	3	Capillary disappeared and reappeared

changes in caliber of capillaries is dependent on passive response to alterations of the pressure of the blood supplying them. There is, however, evidence to show that cells which are not as highly differentiated as muscle cells can respond actively to stimulation. The melanophore of Fundulus heteroclitus responds to adrenalin (31), and to other kinds of stimuli (32). The writer himself has observed changes of form of pigment cells in the skin of frogs and tadpoles.

If an amoeba be stimulated with an electric current, that side of the body of the amoeba which is directed toward the anode contracts (33), then a pseudopodium starts out somewhere on the side directed toward the cathode. There are many other examples of active contraction of very simple forms of protoplasm, and therefore, if in the absence of muscular coats, a protoplasmic unit, such as the amoeba, has the power of active response—changing its form and producing a protrusion,—why should not the property of contraction be possessed by the protoplasm of endothelial cells?

Is capillary constriction an active process? The old conception was that a narrowing of the capillary lumen is an elastic phenomenon, a passive process, which occurs when there is decreased blood pressure in the capillaries, which is caused by constriction of arterioles, or by a low general blood pressure. There is no doubt of the elasticity of capillaries, and that a lowering of internal pressure would tend to cause the lumen to narrow. This does not always take place, however. Roy and Brown (20), by tapping the abdomen of a frog, lowered its central blood pressure, and the pressure in the peripheral arterioles to nearly that of the atmosphere, but the capillaries did not change their size. They also mentioned that on amputating a frog's foot, the capillaries became very little narrower, although the pressure had been reduced to zero. When the writer cut a capillary net work—nearly free from arteries and veins—from an isolated scale of Fundulus, the capillaries did not change in caliber, although the blood pressure had been decreased. Dale and Laidlaw (4) proved that histamine causes a constriction of the arterioles and that this constriction did not prevent the widespread dilatation of capillaries. Heubner (22) has shown that the intravenous injection of the double chloride of gold and sodium produces a shock-like prostration. Microscopically, venules and capillaries of all the tissues were found to be dilated, but the small arteries were so strongly constricted as to occlude the lumina completely. It is evident that the narrowing of the lumen of the capillary does not depend simply on the pressure of the blood supplied to it, and that capillary response may be independent of arterial activity.

The writer, as has been stated in the description of his experiments, observed the constriction of a single capillary, even a part of a blood capillary, to take place without any recognizable change of immediately surrounding vessels. The change of the capillary wall was also indicated by the character of the flow of the blood corpuscles. Using a microscope giving a high magnification, a change of shape of corpuscles passing the stimulated part of a capillary was distinctly observed. The most suitable place for applying stimulation was the middle of a long capillary. With an appropriate stimulation, the arteriole, the venule, and parts of the capillary on both sides of the stimulated point remained unaltered. A corpuscle, when travelling the arteriole and a part of the capillary, showed its usual shape, but when it came to the excited part, it exhibited various forms, one after another (see fig. 4). When it reached the part of the same capillary beyond the excited region, it resumed its ordinary form.

The writer would like to emphasize that not only the capillaries of animals, but also of the human skin, can respond to adequate stimuli. In the case of human capillaries, as has been shown by his experiments, the reaction, such as a slowing of the corpuscular flow, a disappearance, or a change of appearance of the stimulated capillary, could not be due simply to a constriction of arterioles, because the response was usually very localized. It seems as if there is no doubt that the capillary constriction is an active response.

Is the capillary dilatation dependent simply on a rise of blood pressure? The writer believes that it is a change in the condition of the capillary wall itself that causes the dilatation, and that the capillaries are not enlarged or opened up simply by an internal pressure. As Krogh (1) has pointed out, the arterial pressure is unable to dilate capillaries to any appreciable degree, or to open them up when tonically constricted, while the venous pressure may be sufficient to fill them when relaxed in response to local stimulation. If the opening up of capillaries be merely a passive proccess, then those with least resistance would always have an easier chance. If this be the case, the blood would always flow through the same definite channels when the capillary pressure is low, and the distribution of oxygen and nutritive substances would be very unequal, the cells lying nearest to the open capillaries being well supplied, while those at the greatest distance were starved. He has also added that the pressure necessary to force muscle capillaries open when they are actively contracted is much higher than the normal arterial pressure.

The evidence that capillaries are not simply passively expanded by the increased intracapillary pressure, which results from an arteriole dilatation, or from a rise of general arterial pressure, comes from many sides. For instance, in Stricker's experiments, the nictitating membrane of a frog was removed from the body and therefore deprived of its blood supply, yet an evident dilatation of the capillaries could still take place. Roy and Brown (20) have shown that with a very low capillary pressure, capillaries remain dilated by the application of chloroform. The writer has applied chloroform to an isolated capillary net work of Fundulus, dilatation of capillaries in response to chloroform was still present, in spite of the fact that there must have been very little pressure either in the arterial or the venous sides. Again as pointed out by Roy and Brown (20) in the case of hyperemia, which follows temporary anemia, also, the dilated capillaries remain expanded, although by the "Klopfversuch" their internal pressure has been reduced to only a little above

zero. Moreover, Dale and Laidlaw (4) have shown that histamine causes a widespread dilatation of capillaries of cats, independent of its effect on arterioles, which are constricted. Krogh (25) has found that urethane causes dilatation of capillaries without affecting the arteries. He concludes that capillary dilatation is independent of blood pressure.

The writer has noted several cases of very localized dilatation. This was not only independent of arterial dilatation, but also independent of the condition of the rest of the same capillary. The point under observation was larger than the rest of the vessel, moreover, the blood stream passing through it became gradually slower, and at last that part became packed with corpuscles. If it was simply expanded passively by intracapillary pressure, why did not the pressure expand the rest of the capillary? The observations suggested that the reaction was associated with a vital response.

Are endothelial cells the agents of the active response of blood capillaries? Stricker (14), Roy and Brown (20), Dale and Laidlaw (4), Hooker (34) and Krogh (1) have the opinion that the endothelial cells are responsible for the capillary phenomena. On the other hand, Rouget (16) and Steinach and Kahn (21) had the view that certain perivascular elements caused the capillary constriction. As has been pointed out by Hooker (38), the vessels which they regarded as capillaries, were probably arterioles. Working with a microscope of very high power, the writer observed extremely clear pictures of the endothelial cells and their nuclei, of the capillaries of the fin expansion of tadpoles, but failed to see any such perivascular elements, yet these vessels contracted when locally excited.

There might be two possibilities: *a*, contraction of the endothelial cells of the type to narrow the lumen so that the blood would cease to enter; *b*, bulging of the endothelial cells, so that the lumen of the capillary would be encroached on enough to prevent the entrance of the blood. In the case of human capillaries, the vessels were not observed as such, but by their contained blood. In the case of the bat's wing, sometimes the outline of the capillary wall was shown, though at other times it was not seen even when the blood was flowing. In the latter case,when the blood ceased to enter the capillary, the indication of the presence of a capillary ceased.

The alteration of the shape of individual corpuscles, which the writer also observed, when they were passing, one by one, a stimulated part of a capillary (fig. 4) would suggest that the excitation might cause a bulging out of a part of the endothelial protoplasm to block the capillary

lumen partially; or that the phenomenon might be due to a contraction of the endothelial cells of such a type as to make the capillary lumen irregular. The experimental facts, therefore, tended to show that the endothelial cells were the agents of the active response of the blood capillary.

SUMMARY AND CONCLUSIONS

The unipolar method of electrical stimulation was employed to study the effect of direct, localized excitation on the blood capillaries of frogs, tadpoles, fish, bats, and men. Their active response was detected by observation with the microscope.

Induced as well as direct currents were employed. Single make and break shocks did not cause visible effects; a summating series was required to elicit a response.

Capillaries of the web of frogs and of the caudal fin of fish respond to a tetanizing current, and to a series of induction shocks. They also responded to the direct current, when a series of excitations was employed.

Capillaries of the bat's wing were seen to respond only once to a tetanizing current, but they reacted to separate induction shocks and to the direct current.

Capillaries of the human skin did not react to a tetanizing current, but responded to separate induction shocks. They reacted also to the direct current when a series of excitations was used.

Capillaries of the same tissue, stimulated in the same manner, gave various effects concerning the latent period, the duration of contraction, of slowing of flow, stopping of flow and disappearance of capillaries.

When the capillaries of the bat's wing were studied under a high power, a change of shape of individual corpuscles passing through a stimulated part was observed.

That the blood capillaries respond to stimulation actively, that both capilo-constriction and capilo-dilatation are active responses, and that the capillary endothelium is responsible for the phenomenon have been suggested by experimental results. The fact that the reaction to stimulation was strictly localized, would seem to justify the conclusion that the result was an active response of the wall of the capillary.

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